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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/972,268	10/05/2001	Peter R. Baum	3101-A	4855

22932 7590 12/31/2002

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EXAMINER	
HADDAD, MAHER M	
ART UNIT	PAPER NUMBER
1644	12

DATE MAILED: 12/31/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/972,268	BAUM ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11, 19 amd 54-58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11, 19 amd 54-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6&10* .
4) ☒ Interview Summary (PTO-413) Paper No(s). *11* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1-11, 19, and 54-58 are pending.

2. Applicant's election with traverse of Group III, claims 1-11 and 19 (now 1-11, 19 and 54-58) drawn to a substantially purified polypeptide comprising an amino acid sequence that of SEQ ID NO: 6 and amino acid 74-152 thereof as the species, filed on 10/29/02, is acknowledged.

Upon reconsideration Examiner has extended the search to cover SEQ ID NO: 2, 4, 6, 8, 10, 12, and 31.

3. Claims 1-11, 19 and 54-58 are under examination as they read on a substantially purified polypeptide comprising an amino acid sequence that of SEQ ID NO: 2, 4, 6, 8, 10, 12, and 31 and amino acid 74-152 thereof as the species.

4. Applicant's IDS, filed 5/28/02 and 10/28/02 (Paper No. 6 and 10, respectively), is acknowledged, however, reference 1B was crossed out and was considered only in regard to the Abstract as the English translation was not found. Applicant is invited to produce the English translation of document.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1, 2, 4-8, 10, 11, 19 and 54 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 1, 2 and 4 are indefinite in the recitation "polypeptide comprising an amino acid" in line 1, and "a polypeptide consisting of said amino acid" in line 3, 4 and 5, respectively. It is unclear whether the polypeptide is "comprising" or "consisting of" an amino acid.

B. Claims 6 and 8 are indefinite for reciting "from about amino acid 74 to152". It is unclear how many amino acids constitute "about". One of skill in the art would not know if applicant meant 4 amino acid, as many as 11 amino acids, or even more.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-10, 11, 19 and 54-58 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a substantially purified polypeptide comprising an amino acid of SEQ ID NO: 2, 4, 6, 8, 10, 12 and 31, wherein SEQ ID NO:4, 6, 10, 12, and 31 comprising amino acids 74-152, wherein the polypeptide consisting of amino acid sequence that binds to nectin-1 for inhibiting endothelial cell migration; does not reasonably provide enablement for any substantially purified polypeptide **comprising** an amino acid sequence that is at least 80% or 90% identical to at least 20 contiguous amino acids of the extracellular domain or a sequence selected from the group consisting of SEQ ID NO: 2, 4, 6, 8, 10, 12 or 31 in claims 1-2 and 4-5(a) or any amino acid sequence of the extracellular domain that inhibits endothelial cell migration in claim 4-5(b), any substantially purified polypeptide **comprising** any amino acid fragment of an amino acid sequence of SEQ ID NO: 2, 4, 6, 8, 10, 12 or 31 in claim 3(b), or **comprising** an amino acid sequence from amino acid 74-154 of SEQ ID NO: 2, 4, 6, 10, 12 or 31, or any fragment thereof, in claim 6(a-c); any soluble polypeptide of the extracellular domain further comprising a leucine zipper polypeptide, an Fc polypeptide or a peptide linker in claim 7, the soluble polypeptide comprising a sequence Z1-X-Z2, wherein Z1 and Z2 are each individually the amino acid 74-152, or any fragment thereof, and X is a peptide linker in claim 8, or a composition comprising any polypeptide, wherein the soluble polypeptide of claim 4 **comprises** a sequence of SEQ ID Nos:13-16 in claim 9 or a soluble polypeptide and a pharmaceutically acceptable carrier in claims 10 and 11; any polypeptide produced by culturing a recombinant host cell genetically engineered to contain a polynucleotide encoding the polypeptide of calim 4 under conditions promoting expression of said polypeptide in claim 19; any substantially purified polypeptide **comprising** amino acids 74-152 in claim 55; any substantially purified polypeptide that binds nectin-1 and **comprises** an amino acid sequence that is at least 80% identical to amino acids 74-152 of SEQ ID NO: 2, 4, 6, 10, 12 or 31in claim 56, any polypeptide or any soluble polypeptide produced by culturing a recombinant host cell wherein said polypeptide **comprises** amino acids 74 through 152 of SEQ ID NO: 2, 4, 6, 10, 12 or 31, or any fragment thereof in claims 19 and 57, wherein the polypeptide or the soluble polypeptide is produced by a method further comprising substantially purifying said polypeptide in claims 54 and 58. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification does not provide a sufficient enabling description of the claimed invention. The specification discloses SEQ ID NO: 2, 4, 6, 8, 10, 12 and 31 with a disclosed activity of inhibiting endothelial cell migration (e.g., page 54 under Modulation of endothelial cells migration by soluble human nectin-3). The instant claims encompass in their breadth *any* amino acid "with at least about 80 or 90 % identity to at least 20 contiguous amino acids of SEQ ID NO: 2, 4, 6, 8, 10, 12 or 31"; or *any* amino acid "that is at least about 80 % identity to amino

acids 74 through 152 of SEQ ID NO: 4, 6, 10, 12, or 31" or " that is at least about 80 or 90 % identity to at least 20 contiguous amino acids of SEQ ID NO: 2, 4, 6, 10, 12 or 31", including those that comprise a "fragments" of amino acids 74-152 of SEQ ID NO: 2, 4, 6, 10, 12 and 31 (a polypeptide *comprises a fragment of amino acids 74-154*)., or any polypeptide comprising amino acids 74-152, or any soluble polypeptide comprises SEQ ID NO:13-16.

However, there does not appear to be sufficient guidance in the specification as filed as to how the skilled artisan would make and use the various amino acids recited in the instant claims. A person of skill in the art would not know which sequences are essential, which sequences are non-essential, and what particular sequence lengths identify essential sequences. There is insufficient guidance to direct a person of skill in the art to select particular sequences or sequence lengths as essential for inhibiting endothelial cell migration. Without detailed direction as to which amino acid sequences are essential to the function of the polypeptide, a person of skill in the art would not be able to determine without undue experimentation which of the plethora of amino acid sequences encompassed by the instant claims would share the ability to inhibit endothelial cell migration of the polypeptide of SEQ ID NO: 2, 4, 6, 10, 12 or 31, other than the amino acid of SEQ ID NO: 2, 4, 6, 8, 10, 12 or 31.

Attwood (Science 2000; 290:471-473) teaches that "[i]t is presumptuous to make functional assignments merely on the basis of some degree of similarity between sequences. Similarly, Skolnick et al. (Trends in Biotech. 2000; 18(1):34-39) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2). Finally, even single amino acid differences can result in drastically altered functions between two proteins. For example, Metzler et al. (Nature Structural Biol. 1997; 4:527-531) show that any of a variety of single amino acid changes can alter or abolish the ability of CTLA4 to interact with its ligands CD80 and CD86 (e.g., summarized in Table 2). Thus it is unpredictable if any functional activity will be shared by two polypeptides having less than 100% identity over the full length of their sequences.

The skilled artisan would not reasonably expect a polypeptide having anything less than 100% identity *over the full length of SEQ ID NO: 2, 4, 6, 10, 12 or 31 to share the same function*. The limitation "binds to nectin-1" is not seen as providing a requisite functional activity for the polypeptide because even if the polypeptide binds to nectin-1, there are still numerous functional activities encompassed besides binding to nectin-1. Thus the recitation of percent identity language, in the absence of *a testable function* and limitations regarding the *sequence length over which the percent identity is required*; does not allow the skilled artisan to make and use the encoding nucleic acids commensurate in scope with the instant claims without undue experimentation.

The terms "comprising" and "comprises" in claims 1-3, 6, 9 and 55-57 are open-ended, they expand the amino acid fragments of SEQ ID NO: 2, 4, 6, 8, 10, 12 or 31 to include additional non disclosed amino acids outside of the "at least 20 contiguous amino acids" or any other fragment. The instant claim language appears to encompass fragments. For example, claim 1 recites a polypeptide comprising *an amino acid sequence that is at least 80% identical to at least 20 contiguous amino acids* of SEQ ID NO: 2, 4, 6, 8, 10, 12 or 31. Similarly, claim 6 recites a polypeptide comprises a fragment of amino acids 74-152 of SEQ ID NO: 2, 4, 6, 10, 12 or 31, while claim 9 recites any soluble polypeptide that comprises the fusion protein of SEQ ID NO: 13-16. Such a recitations do not require that the amino acid comprises the full length sequence set forth in SEQ ID NO: 2, 4, 6, 10, 12 or 31; but rather encompasses any amino acid sequence comprising either the full length of SEQ ID NO: 2, 4, 6, 8, 10, 12 or 31or *any fragment.* However, the specification does not appear to have provided sufficient guidance as to which fragments of SEQ ID NO: 2, 4, 6, 8, 10, 12 or 31 would share the function of inhibiting endothelial cell migration. Neither does the specification appear to have provided any working examples of any functional fragments. Thus it would require undue experimentation of the skilled artisan to determine which fragments of SEQ ID NO: 2, 4, 6, 8, 10, 12 or 31 have the function of the full length molecule.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. Without sufficient guidance, the changes which can be made in the instantly recited polypeptide that maintains the functional properties of the polypeptide of SEQ ID NO: 2, 4, 6, 8, 10, 12 or 31 is unpredictable, as is the identity of which fragments would encode a functional polypeptide; thus the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

9. Claims 1-10, 11, 19 and 54-58 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of a substantially purified polypeptide comprising an amino acid of SEQ ID NO: 2, 4, 6, 8, 10, 12 and 31, wherein SEQ ID NO:4, 6, 10, 12, and 31 comprising amino acids 74-152, wherein the polypeptide consisting of amino acid sequence that binds to nectin-1 for inhibiting endothelial cell migration.

Applicant is not in possession of any substantially purified polypeptide comprising an amino acid sequence that is at least 80% or 90% identical to at least 20 contiguous amino acids of the extracellular domain or a sequence selected from the group consisting of SEQ ID NO: 2, 4, 6, 8, 10, 12 or 31 in claims 1-2 and 4-5(a) or any amino acid sequence of the extracellular domain that inhibits endothelial cell migration in claim 4-5(b), any substantially purified polypeptide comprising any amino acid fragment of an amino acid sequence of SEQ ID NO: 2, 4, 6, 8, 10, 12 or 31 in claim 3(b), or comprising an amino acid sequence from amino acid 74-154 of SEQ

ID NO: 2, 4, 6, 10, 12 or 31, or any fragment thereof, in claim 6(a-c); any soluble polypeptide of the extracellular domain further comprising a leucine zipper polypeptide, an Fc polypeptide or a peptide linker in claim 7, the soluble polypeptide comprising a sequence Z1-X-Z2, wherein Z1 and Z2 are each individually the amino acid 74-152, or any fragment thereof, and X is a peptide linker in claim 8, or a composition comprising any polypeptide, wherein the soluble polypeptide of claim 4 comprises a sequence of SEQ ID Nos:13-16 in claim 9 or a soluble polypeptide and a pharmaceutically acceptable carrier in claims 10 and 11; any polypeptide produced by culturing a recombinant host cell genetically engineered to contain a polynucleotide encoding the polypeptide of calim 4 under conditions promoting expression of said polypeptide in claim 19; any substantially purified polypeptide comprising amino acids 74-152 in claim 55; any substantially purified polypeptide that binds nectin-1 and comprises an amino acid sequence that is at least 80% identical to amino acids 74-152 of SEQ ID NO: 2, 4, 6, 10, 12 or 31in claim 56, any polypeptide or any soluble polypeptide produced by culturing a recombinant host cell wherein said polypeptide comprises amino acids 74 through 152 of SEQ ID NO: 2, 4, 6, 10, 12 or 31, or any fragment thereof in claims 19 and 57, wherein the polypeptide or the soluble polypeptide is produced by a method further comprising substantially purifying said polypeptide in claims 54 and 58.

Applicant has disclosed only amino acids of SEQ ID NO: 2, 4, 6, 10, 12 or 31; therefore, the skilled artisan cannot envision all the contemplated amino acid sequence possibilities recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-7, 10, 11, 19 and 54-58 are rejected under 35 U.S.C. 102(a) as being anticipated by Reymond *et al* (Gene 255:347-355, Sept 2000) (IDS Ref. No. 1C).

Reymond *et al* teach an isolated nectin3/PRR3 polypeptide comprising 100% identical to claimed SEQ ID NO: 2 and 6 comprising an amino acid sequence that is 100% identical to at least 79 contiguous amino acids of a sequence at positions 74-152 of SEQ ID NO: 2 (aa positions 67-145), 4, 6, 8 (aa positions 68-146), 10, 12 and 31, wherein a polypeptide consisting of said amino acid sequence binds to nectin-1 (see page 350, figure 1 in particular). The polypeptide further comprising a fragment of an amino acid sequence that binds to nectin-1. Reymond *et al* further teach that the PRR3 protein was transiently expressed in Cos1 cells and immunoprecipitated (purified) using anti Flag M2 mab or antipeptide serum directed to the C-terminal portion of PRR3 (see pages 349-350 under Identification of PRR3 protein in a transient expression system in particular). Finally, Reymond *et al* teach Flag-PRR3 protein (see Fig 3 on page 352 in particular) as a polypeptide comprising a peptide linker. The term "comprising" in claims 1-7, 55-57 is open ended, it would open the claims to include the reference 549 amino acid sequence. It is noted that amino acids 1-404 of SEQ ID NO: 6 and amino acids 1-366 of SEQ ID NO: 12 read on extracellular domain.

Claims 10 and 11 are included because Reymond *et al* teach the protein complex in buffer which is considered to be a pharmaceutically acceptable carrier (see page 349, under immunoprecipitation and Western blotting analyses in particular).

The reference teachings anticipate the claimed invention.

12. Claims 1-6, 19, 54 and 57-58 are rejected under 35 U.S.C. 102(b) as being anticipated by Ottenwelder *et al* (GenBank Accession No. T08732, 1999).

Ottenwelder *et al* teach a 407 amino acid polypeptide comprising an amino acid sequence that is 100% identical at least 20 contiguous amino acids of a sequence at amino acid positions 136-464 of SEQ ID NO: 2, aa 143-464 of SEQ ID NO: 4 and 6, aa 137- 351 of SEQ ID NO: 8, aa 143-357 of SEQ ID NO: 10, 12 and 31 (sequence alignment in particular). The polypeptide further comprises a fragment of an amino acid sequence of SEQ ID NO 2, 4, 6, 8, 10, 12, or 31 and fragment of amino acid 74-152 of SEQ ID NO 2 (at positions 67-145), 4, 6, 8 (at positions 68-146), 10, 12, or 31 as claimed in claim 6. The term "comprising" in claims 1-6 and 57 is open ended, it would open the claims to include the reference 407 amino acid sequence. It is noted that amino acids 1-404 of SEQ ID NO: 6 and amino acids 1-366 of SEQ ID NO: 12 read on extracellular domain.

Claims 19, 54 and 57-58 are included because Ottenwelder *et al* teach polypeptide comprising a fragment or soluble polypeptide and product is a product irrespective of how it is produced or purified.

While the prior art teachings may be silent as to the "amino acid sequence binds to nectin-1" or "inhibits endothelial cell migration" per se; the product used in the reference is the same as the claimed product. Therefore "amino acid sequence binds to nectin-1" and "inhibits endothelial cell migration" are considered inherent properties.

The reference teachings anticipate the claimed invention.

13. Claims 1-7, 10, 11, 19, 54 and 56 are rejected under 35 U.S.C. 102(a) as being anticipated by Satoh-Horikawa et al (J. of Biol. Chem. 275:10291-10299, April 2000) (IDS Ref. No. 10C).

Satoh-Horikawa et al teach three isolated nectin3 polypeptides, nectein-3α (549aa), 3β (510aa) and 3γ (438 aa) comprising an amino acid sequence that is 98.6% identical to at least 79 contiguous amino acids of a sequence at amino acid positions 74-152 of SEQ ID NO: 2 (aa positions 67-145), 4, 6, 8 (aa positions 68-146), 10, 12 and 31 (see page 10292, figure 1 and the attached sequence alignment in particular). The said nectin3 polypeptides comprising an amino acid fragment of SEQ ID NO:2, 4, 6, 8, 10, 12, or 31 (see sequence alignment in particular) as recited in instant claim 6. Satoh-Horikawa et al teach a FLAG-nectin 3α (aa 56-549), FLAG-nectin 3β (aa 56-510) FLAG-nectin 3γ (aa 56-438), Fc-nectin 3α-EX (aa 56-400) as in the instant claim 7 (see page 10292 under construction and purification), The term "comprising" in claims 1-5 and 56 is open ended, it would open the claims to include the reference 549, 510 and 438 amino acid sequences. It is noted that amino acids 1-404 of SEQ ID NO: 6 and amino acids 1-366 of SEQ ID NO: 12 read on extracellular domain.

Claims 10-11 are included because Satoh-Horikawa et al teach the proteins in PBS containing 20 mM maltose and 0.1% Triton X-100 which is consider to be a pharmaceutically acceptable carrier (see page 10293, under Affinity chromatography in particular).

While the prior art teachings may be silent as to the "amino acid sequence binds to nectin-1" or "inhibits endothelial cell migration" per se; the product used in the reference is the same as the claimed product. Therefore "amino acid sequence binds to nectin-1" and "inhibits endothelial cell migration" are considered inherent properties.

The reference teachings anticipate the claimed invention.

14. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Reymond et al, Ottenwelder et al or Satoh-Horikawa et al each in view of U.S. Patent No. 6,472,520.

The teachings of Reymond et al, Ottenwelder et al and Satoh-Horikawa et al references have been discussed, supra.

The claimed invention differs from the reference teachings only by the recitation that the soluble polypeptide further comprising a leucine zipper polypeptide, an Fc polypeptide or a peptide linker in claim 7.

The `520 patent teaches a polypeptide can comprise a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (e.g., poly-His or hemagglutinin), or to enhance binding of the polypeptide to a solid support. Fusion proteins capped with such peptides may also be resistant to intracellular degradation in E. coli. Protein fusions, for example, polypeptides conjugated to an immunoglobulin Fc region or a leucine zipper domain (Column 45, lines 43-55 in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to fuse the soluble polypeptide taught by Reymond et al, Ottenwelder et al or Satoh-Horikawa et al with peptide linker, an Fc or a leucine zipper domain as taught by the `520 patent.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because such fusion polypeptide are use for ease of synthesis, purification or identification of the polypeptide, or to enhance binding of the polypeptide to a solid support as taught by the `520 patent.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

15. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Reymond et al, Ottenwelder et al or Satoh-Horikawa et al each in view of U.S. Patent No. 6,362,371.

The teachings of Reymond et al, Ottenwelder et al and Satoh-Horikawa et al references have been discussed, supra.

The claimed invention differs from the reference teachings only by the recitation that the soluble polypeptide comprising a sequence Z1-X-Z2, wherein Z1 and Z2 are each individually the amino acid 74-152 of SEQ ID NO: 4, 6, 10, 12, or 31, a fragment of said amino acid 74-152 and X is a peptide linker in claim 8.

The `371 patent teaches bivalent interactions of dimeric compounds bearing two copies of the same ligand joined to a single linker. The `371 patent further teach that the dimeric compound are more potent and selective antagonist and a superior therapy urge incontinence (Column 38, lines 41-43 and 58-60 in particular). The `371 patent further teaches that linkers can be Amide bonds (peptide bonds), ethers, amines, carbamates, ureas, and sulfonamides (Column 39, lines 1-3 in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to link the soluble polypeptide taught by Reymond et al, Ottenwelder et al or Satoh-Horikawa et al using the protein linker as taught by the `371 patent to obtain a dimer.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the dimeric compound are more potent and selective antagonist and a superior therapy urge incontinence as taught by the `371 patent.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

16. No claim is allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad, whose telephone number is (703) 306-3472. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600
December 30, 2002

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